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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	)	
	)	
Blackshear et al.	)	Group Art Unit: 1634
	)	
Application No. 10/049,586	)	Examiner: Sisson, B. L.
	)	
Filing Date: February 12, 2002	)	Confirmation No.: 9700
	)	
For: TTP-RELATED ZINC FINGER DOMAINS AND METHODS OF USE	)	

APPEAL BRIEF

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

NEEDLE & ROSENBERG, P.C.
Customer Number 36339

Sir:

This is an appeal from the non-final rejection of claims 53-61, 71, and 72 in the Office Action mailed May 11, 2006, in the above-identified patent application. Each of these claims has been twice rejected. A Notice of Appeal was mailed on October 9, 2006.

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(1) REAL PARTY IN INTEREST

The real party in interest of this application is The Government of the United States of America, as represented by the Secretary, Department of Health and Human Services.

(2) RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences known to Appellants, the undersigned, or Appellants' assignee which directly affects, which would be directly affected by, or which would have a bearing on the Board's decision in this appeal.

(3) STATUS OF CLAIMS

Claims 53-61, 71, and 72 are pending. Claims 1-52, 62-70 have been cancelled. Claims 53-61, 71, and 72 have been twice rejected and are on appeal. The text of each claim on appeal, as pending, is set forth in an Appendix to this Appeal Brief.

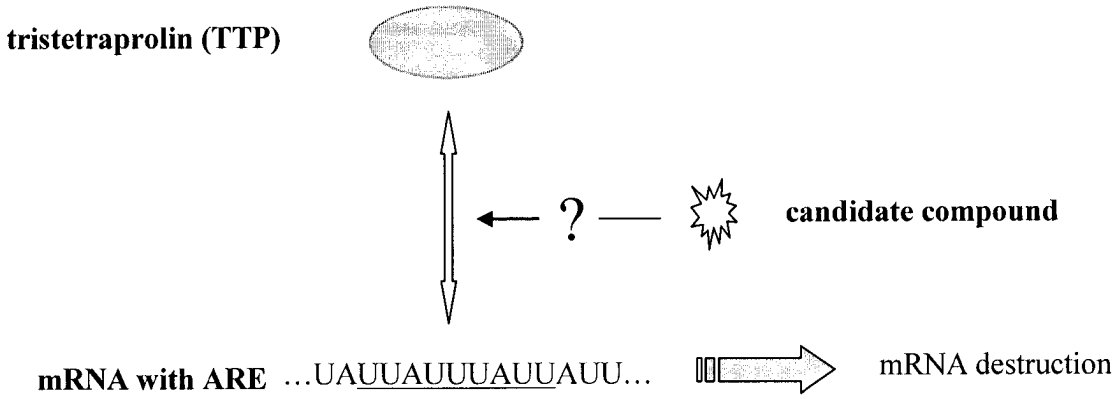
(4) STATUS OF AMENDMENTS

No amendments after final rejection have been filed.

(5) SUMMARY OF CLAIMED SUBJECT MATTER

The claims on appeal are drawn to a method of identifying a compound that modulates the binding of a tristetraprolin (TTP) or a TTP-like polypeptide to an AU-rich element (ARE). This method is based upon the discovery that TTP and TTP-related proteins stimulate the destruction of certain mRNAs by binding to an AU-rich element (ARE) within the 3' untranslated region of such mRNAs, and that the zinc finger domain of TTP and TTP-related proteins is sufficient to mediate this destruction. For example, mRNAs encoding polypeptides such as tumor necrosis factor-alpha (TNF-α), granulocyte-macrophage colony stimulating factor (GM-CSF), and interleukin-3 (IL-3) all contain such AREs and are destabilized by the binding of TTP and TTP-like polypeptides to the ARE. Thus, the present claims are drawn to methods of identifying compounds that are useful for regulating degradation of ARE-containing mRNAs

that encode polypeptides involved in disease and inflammation. An illustration of this method is shown below:



Independent claim 53 and the dependent claims on appeal focus on three features:

(1) a sample containing the TTP or the TTP-like polypeptide and an ARE (which is described at least on page 18, lines 5-18 and exemplified on page 64, lines 6 to 23 and page 71, lines 7 to 26),

(2) contacting the sample with a candidate compound (paragraph bridging pages 6 and 7), and

(3) detecting or measuring the binding between the ARE and the TTP or TTP-like polypeptide (which is described at least on page 30, line 8 to page 31, line 11).

Thus, all the practitioner must provide is a candidate compound to be tested by the method. To this end, examples of types of candidate compounds are provided on page 31, line 13 to page 32, line 8 of the specification.

(6) GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The issues presented on appeal are: (1) whether claims 53-61, 71, and 72 are enabled as required by 35 U.S.C. § 112, first paragraph; (2) whether claims 53-61, 71, and 72 are supported by a credible asserted utility or well-established utility as required by 35 U.S.C. §101; and (3) whether claims 53-61, 71, and 72 are supported by a credible asserted utility or well-established utility as required by 35 U.S.C. § 112, first paragraph.

(7) ARGUMENT

(A) Rejection of Claims 53-61, 71, and 72 Under 35 U.S.C. § 112, first paragraph, as not being enabled

Claims 53-61, 71, and 72 stand rejected under 35 U.S.C. § 112, first paragraph, as not being enabled. Appellants respectfully traverse this rejection.

(i) The Issues

Appellants submit that the present rejection depends only on the question of whether, in view of the specification and the knowledge of those of skill in the art at the time the invention was made (as evidenced by the complete record in this application), the method of claims 53-61, 71, and 72 could be practiced by those of skill in the art without the need for undue experimentation.

The Examiner contends that the specification does not enable those of skill in the art to practice the claimed method mainly on the basis that none of the examples is drawn to the claimed method. The Examiner further contends that the specification is essentially silent as to appropriate combinations of starting materials and reaction conditions for even one embodiment of the claimed invention.

Appellants assert that the specification *does* enable the steps to be used in the claimed method according to the legal standard for the enablement of a screening method. Appellants further submit that the present rejection fails to properly consider what needs to be described in view of what is claimed and fails to properly apply the enablement requirement as it applies to a screening method, and fails to properly apply that law to the claimed method.

(ii) The Legal Standard

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the specification, coupled with information known in the art, without undue experimentation. See United States v. Telectronics, Inc., 857 F.2d 778, 8 USPQ2d 1217 (Fed. Cir. 1988); In re Stephens, 529 F.2d 1343, 199 USPQ 659 (CCPA 1976). Determining enablement is a question of law based on underlying factual findings. In re Vaeck, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991); Atlas Powder Co. v. E.I. duPont de Nemours & Co., 750 F.2d 1569, 224 USPQ 409 (Fed. Cir. 1984).

It is axiomatic that only that which is actually claimed need be enabled. See Christianson v. Colt Industries Operating Corp., 822 F.2d 1544, 1562, 1 USPQ2d 1241, 1255 (Fed. Cir. 1987) ("The 'invention' referred to in the enablement requirement of section 112 is the *claimed* invention")(hereafter "Christianson I"); Christianson v. Colt Industries Operating Corp., 870 F.2d 1292, 1299, 10 USPQ2d 1352, 1357 (7th Cir. 1989) ("Because only the claimed invention receives patent law protection, the disclosures need generally be no greater than the claim.")(hereafter "Christianson II"). There is no requirement that the claimed method be actually demonstrated in order to meet requirements of 35 U.S.C. § 112, first paragraph. See Gould v. Quigg, 822 F.2d 1074, 1078, 3 USPQ2d 1302, 1304 (Fed. Cir. 1987) (the mere fact that something has not previously been done is not, in itself, a sufficient basis for rejecting all applications purporting to disclose how to do it). A patent need not teach, and preferably omits, what is well known in the art. See Spectra-Physics, Inc. v. Coherent, Inc., 827 F.2d 1524, 3 USPQ2d 1737 (Fed. Cir. 1987).

(a) Undue Experimentation

Whether undue experimentation is needed to practice a claimed invention is not based upon a single factor, but rather a conclusion reached by weighing many factors. Many of these factors have been summarized in In re Wands, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988) as follows:

(1) The quantity of experimentation necessary (time and expense);

(2) The amount of direction or guidance presented;

(3) The presence or absence of working examples of the invention;

(4) The nature of the invention;

(5) The state of the prior art;

(6) The relative skill of those in the art;

(7) The predictability or unpredictability of the art; and

(8) The breadth of the claims.

A specification complies with the enablement requirement of 35 U.S. C. § 112, first paragraph, if it allows one of skill in the art to make and use the claimed invention without undue

experimentation. See In re Wright, 999 F.2d 1557, 1561, 27 U.S.P.Q.2d 1510,1513 (Fed. Cir. 1993). The examiner has the initial burden of establishing lack of enablement. See id.

The fact that experimentation may be complex does not necessarily make it undue if the art typically engages in such experimentation. See M.I.T. v. A.B. Fortia, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985). The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. See In re Angstadt, 537 F.2d 498, 190 USPQ 214 (CCPA 1976).

> The test [for undue experimentation] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed.

PPG Indus., Inc. v. Guardian Indus. Corp., 75 F.3d 1558, 1564, 37 U.S.P.Q.2d 1618, 1623 (Fed. Cir. 1996)(internal quotes and citation omitted).

(b) Burden in Making Enablement Rejection

The standard for making a rejection based on 35 U.S.C. § 112, first paragraph, is articulated in In re Wands, 858 F.2d 731 (Fed. Cir. 1988) (see also MPEP § 2164.01 and 2164.04). Initially, the Patent Office must accept the objective truth of statements made in the specification. If such statements are to be called into question, the Patent Office is burdened with providing evidence or convincing argument why those of skill in the art would doubt the statements. See In re Marzocchi, 439 F.2d 220, 169 USPQ 367 (CCPA 1971). Applicant need not present counter evidence if the Patent Office fails to meet this burden. *See id.*

(iii) The Specification, in Combination with the Knowledge and Skill of Those of Skill in the Art, Enables Any Person Skilled in the Art to Make and Use the Subject Matter of Claims 53-61, 71, and 72

As discussed above, the present rejection depends only on the question of whether, in view of the specification and the knowledge of those of skill in the art at the time the invention was made (as evidenced by the complete record in this application), the method of claims 53-61, 71, and 72 could be practiced by those of skill in the art without the need for undue experimentation. Appellants assert that the answer to this question is *yes*.

Appellants need only enable what is actually claimed. See Christianson I, 822 F.2d at 1562; Christianson II, 870 F.2d at 1299. Thus, in assessing whether undue experimentation would be required to practice the claimed method, it is important to focus on what would actually have to be done in order to practice the method. The steps of the present methods include:

(1) starting with a sample containing the TTP or the TTP-like polypeptide and an ARE (which is described at least on page 18, lines 5-18 and exemplified on page 64, lines 6 to 23 and page 71, lines 7 to 26),

(2) contacting the sample with a candidate compound (paragraph bridging pages 6 and 7), and

(3) detecting or measuring the binding between the ARE and the TTP or TTP-like polypeptide (which is described at least on page 30, line 8 to page 31, line 11).

Appellants submit that they have described the critical materials for the claimed method (e.g., ARE and TTP) and the steps to be used.

As to the sample containing the TTP or the TTP-like polypeptide and an ARE, the specification clearly describes what is meant by TTP, TTP-like polypeptide, and ARE on page 9, line 10 to page 10, line 10. In addition, the minimum sequences for each of these elements is provided on page 18, lines 5-10. Specific examples of TNFα 3'UTR RNA probes comprising an ARE are provided in the Examples on pages 65, line 16 to page 66, line 30 of the specification. Samples containing TTP or TTP-like polypeptide and ARE are provided in the Examples at least on page 64, lines 6 to 23, where TNF-α mRNA from cell extracts and TTP oligonucleotides are combined on a Northern blot, and page 71, lines 7 to 26, where cells are co-transfected with constructs expressing both TTP and TNF-α (comprises an ARE), are described. This describes at least two examples of a combination of starting materials that constitute the assay.

As to the compound, the Appellants disclose in the specification "large libraries of natural products or synthetic (or semi-synthetic) extracts or chemical libraries" that can be screened using the provided screening method (page 31, line 13 to page 32, line 8). However, it should be recognized that the compound referred to in the claims is an object of the claimed method. It is the thing that is being studied by the present screening method. By its very nature a

screening assay anticipates a realm of compounds that cannot be predicted to have any function in the assay before their use in the assay. Further, the skilled person would know that how a compound is delivered (e.g., diluent, pH, concentration, or duration of contact) to an assay system (e.g., ARE + TTP) is dependent upon both the nature of the candidate compound and of the assay being used. The reaction conditions under which contacting can take place are exemplified in the Examples which provide detailed guidance as to the conditions for cell-based and cell-free detection of TTP binding to ARE (TNF- α).

As to the detection step, the Appellants disclose in the specification cell-based and cell-free assays for determining whether a compound interferes with TTP (or related protein) binding to AREs or with mRNA stability. The Appellants again direct the Office to page 30, line 8, wherein the Appellants disclose the following:

> A variety of assay methods can be used to determine whether a given compound interferes with TTP or related protein binding to the GM-CSF ARE and the breakdown of GM-CSF mRNA. These would include cell-based experiments, such as the transfection studies in 293 cells cited in Example 3; it can be seen that addition of cell-permeable compounds to the cells that inhibited the TTP-mRNA interaction would result in inhibition of TTP's ability to deadenylate and destroy the mRNA. Such assays could use a variety of more convenient readouts, e.g. luminescent proteins, human growth hormone, chloramphenicol acetyltransferase, beta-galactosidase, etc. Similar cell based studies could also be performed in yeast, where there is considerable precedent for high-throughput screening assays for protein interactions with DNA, RNA and other proteins. Cell-free assays would probably be the most convenient to set up; these would involve extracts from cells expressing TTP or its related proteins (e.g., ERF1, ERF2, etc.) or its active fragments (e.g., the double zinc finger domain), and testing their ability to bind to purified, labeled GM-CSF ARE, assayed by either crosslinking or gel-shift assays as described in the Examples. More conveniently still, these assays could use purified TTP or its active fragments, or purifed members of the TTP-related protein class or their active fragments, or fusion proteins expressing TTP or its related proteins or their fragments. All have been shown to be active at binding and crosslinking to the TNFα ARE. These would use variable lengths of sequence of the GM-CSF ARE – e.g., a probe that corresponds to bases 3390 – 3467 of Genbank accession number X03020, but the experiments with the TNF ARE have shown that this could probably be shortened to a "core" ARE of about 23 bases (bases 1309 to 1332 of Genbank Accession number X02611and corresponding bases for GM-CSF). (emphasis added)

While the Appellants contend that the method need not be actually practiced in an exemplary protocol to satisfy the enablement requirement, the only step of the method that was not explicitly exemplified was the part of the contacting step that involved the addition of the compound being screened. For example, an analysis of RNA-protein complexes by SDS-PAGE electrophoretic mobility shift assay (EMSA) is provided in the specification (page 65, line 16 to page 68, line 17). This section provides examples of TNFα 3'UTR RNA probes comprising an ARE. This section further provides a protocol for incubating a sample containing TTP protein and the ARE together followed by gel electrophoresis for detecting the binding between the ARE and the TTP (i.e., the formation of RNA-protein complexes). The only step of the provided method not exemplified therein was the contacting step, wherein a candidate compound is added to either the cytosolic extract or the RNA probe prior to their co-incubation. However, this step is both variable and routine. Furthermore, as the choice of compound to apply to the screening method is variable, exemplification of the method, wherein a specific compound is identified and described, could not show definitively that any other compound would likewise be identified. Thus, if, *arguendo*, exemplification were required for enablement, then a provided working example could only be enabling of the use of the method to identify *that* compound. Although this appears to be an implication of the present rejection, Appellants are confident that this is not how the Patent Office intends its analysis of enablement for a screening method to be applied.

(iv) The Examiner's Arguments Are Based on an Incorrect Legal Standard

The Examiner's arguments, and the conclusions drawn therefrom, indicate that the Examiner is applying an incorrect legal standard in assessing enablement of claims 53-61, 71, and 72. The Examiner is requiring that the specification either exemplify the claimed method or be specific as to the exact combinations of starting materials and reaction conditions. Thus, the rejection, *de facto*, requires absolute predictability. However, a determination of non-enablement is not based upon a single factor, but rather is a conclusion reached by weighing many factors. See In re Wands. The factors to be considered for enablement include combinations of:

(1) The quantity of experimentation necessary (time and expense);

(2) The amount of direction or guidance presented;

(3) The presence or absence of working examples of the invention;

(4) The nature of the invention;

(5) The state of the prior art;

(6) The relative skill of those in the art;

(7) The predictability or unpredictability of the art; and

(8) The breadth of the claims.

Thus, it is improper to conclude a lack of enablement without considering all of these factors.

The Examiner's bases for the rejection are the allegations that the specification (1) lacks direction or guidance presented and (2) lacks working examples. First, the Appellants dispute these conclusions. Second, the Examiner has disregarded at least the nature of the invention and the relative skill of those in the art. Third, the Examiner has misrepresented the predictability of the art and the breadth of the claims as being contrary to enablement. Each of these three issues is addressed below.

(v) The Examiner's Evidence and Arguments Do Not Establish that the Subject Matter of Claims 53-61, 71, and 72 are Not Enabled

A Working Example is Not Required and is Not Dispositive

The Examiner argues that because the specification does not provide a working example of the claimed method by identifying a compound that inhibits the binding of a TTP or TTP-like molecule to an ARE, the claimed method is nonenabled. For example, the Office action mailed May 11, 2006 states "[a]s is plainly evident, none of the examples is drawn to the claimed method."

First, the Examiner's conclusion is clearly overstated. As demonstrated above, the only step of the method that is not specifically exemplified is the part of the contacting step that involves the delivery of the compound being tested. For example, Examples 3 and 4 of the specification are clearly directed to methods of determining the binding of TTP or TTP-related proteins to AU-rich elements (see page 65, line 16 to page 68, line 17 of the specification).

Second, while the presence or absence of working examples is a factor to be considered in assessing enablement, as with other Wands factors, it is not conclusive. See Gould v. Quigg, 822 F.2d 1074, 1078, 3 USPQ2d 1302, 1304 (Fed. Cir. 1987) (the mere fact that something has

not previously been done is not, in itself, a sufficient basis for rejecting all applications purporting to disclose how to do it). By the Examiner's logic, the invention of a new method of catching fish using a specially designed fishing pole is not enabled if the specification does not provide a description of the pole in use. In reality, upon description of the pole, the skilled fisherman does not need a description of how to add bait to a hook or where to cast the bait in order to catch a fish. Rather, he needs to know how to make and use the special features of the fishing pole. Similarly, the Appellants need only provide how to make and use the special features of the screening method.

The Examiner has disregarded the nature of the invention and the relative skill of those in the art

While the Appellants may not have been rigidly specific in the description of the compositions and methods that must be used in the screening method, neither does the nature of the invention and the relative skill of those in the art require such specificity. The Appellants disclosed a novel interaction between two molecules and a causative effect of this interaction in a biological system. The nature of the invention is such that the skilled artisan would need only to know (1) how to select TTP polypeptides and oligonucleotides with an ARE, (2) how to detect the interaction of the TTP and ARE, and (3) how to select compounds that might modulate this interaction. Thus, the nature of the experimentation required is neither complex nor atypical for the art of screening compounds. None of these steps required extraordinary skill or knowledge beyond that which was supplied in the specification, namely the identification of TTP and ARE as the starting materials and exemplification of at least one set of contacting and detection conditions (the culture of TTP and TNF-α expressing cells and measurement of the amount of TNF-α encoding RNA.). The specific choice of detection method and reaction conditions requires no more than routine experimentation for optimization. Finally, the nature of the compound to screen is by its very nature impossible to specify *a priori*, since the purpose of the screening method is to identify functionality as a regulator in the disclosed system. One of skill in the art of practicing compound screening would necessarily expect to be responsible for making the selection of compound to screen, and would not expect the provider of the method to

identify the compound. Thus, one of skill in this art would possess the skill to select compounds for use in the method.

The Examiner has misrepresented the predictability of the art and the breadth of the claims as being contrary to enablement

The Examiner indicated on page 8 of the Office action mailed May 11, 2006, that the "breadth of scope claimed" and "unpredictable nature of the art to which the claimed invention is directed" were contrary to enablement. However, no evidence or arguments were presented to support such an assertion. A method for the treatment of disease is often viewed as unpredictable based on the many factors involved in disease progression, *in vivo* delivery, targeting, and half-life. In contrast, a screening method has clearly defined and controlled variables and outcomes. All that is required in the present methods is the ability to detect the modulation of the binding of a TTP to an ARE, which can be by the standard and routine methods described in the specification. The claims do not require this effect on binding to have any therapeutic potential. Thus, the level of predictability that the screening method will work to identify compounds as having or not having the stated effect is extremely high. In fact, the method is so predictable based on the disclosed data that there is no objective basis for challenging its predictability.

Likewise, the breadth of claims is entirely consistent with the requirement of no more than routine experimentation. The elements of the claim that afford breadth include the TTP or the TTP-like polypeptide, the ARE, and the detection of binding step. Each of the TTP/ TTP-like polypeptides and ARE are clearly defined in the specification and exemplified such that the generic description of these starting materials does not significantly affect the amount of experimentation that would be required. And, as discussed above, the detection step is based on routine methods, at least one of which was exemplified in the specification.

(vi) The Examiner's Evidence and Arguments Do Not Establish that the Subject Matter of Claim 54 is Not Enabled

The Examiner notes that the method of claim 54 identifies "a compound that stimulates an activity of a TTP or a TTP-like polypeptide" and argues that the method "does not recite any method steps whereby a correlation in activity is measured." The Examiner uses the example of

hot water, which could denature TTP, as something that could modulate the binding of TTP to an ARE without increasing activity. However, the Examiner has misinterpreted claim 54, which states:

> The method of claim 53, whereby an increase in the binding between the ARE and the polypeptide identifies a compound that stimulates an activity of a TTP or a TTP-like polypeptide.

Quite the opposite of the Examiner's conclusion, the claim recites a method that explicitly correlates an increase in binding between the ARE and the polypeptide with the conclusion that the compound stimulates an activity of a TTP or a TTP-like polypeptide. An example of such an activity, i.e., degradation of mRNA containing an ARE, is exemplified throughout the specification. This ability to stimulate an activity of TTP would be an inherent property of the compound based on its ability to increase the binding of TTP to ARE.

(vii) Conclusion

Appellants assert that the specification *does* enable the steps to be used in the claimed method according to the legal standard for the enablement of a screening method. The Appellants further submit that the present rejection fails to properly consider what needs to be described in view of what is claimed and fails to properly apply the enablement requirement as it applies to a screening method to the claimed method. For at least these reasons, Appellants respectfully request reversal of this rejection.

(B) Rejection of Claims 53-61, 71, and 72 Under 35 U.S.C. § 101, as not having utility

Claims 53-61, 71, and 72 stand rejected under 35 U.S.C. § 101, as not supported by a credible asserted utility or well-established utility. Appellants respectfully traverse this rejection.

(i) The Issues

The Examiner contends that the claimed methods do not have a specific, substantial, and credible utility as required under 35 U.S.C. § 101 mainly on the bases that the claims have allegedly not been exemplified. The Examiner reasons that since the Appellants have not practiced the method and identified a compound that inhibits the binding of a TTP or TTP-like molecule to an ARE, there is no evidence that any such compound can be identified or that such a compound will be useful.

Appellants submit that the present rejection fails to take into account the proper understanding of the utility requirements of a screening method. Appellants assert that (1) the specification *does* enable the steps to be used in the claimed method according to the legal standard for the enablement of a screening method and that (2) a screening method need not be exemplified for the method to have a specific, substantial, and credible utility.

(ii) The Legal Standard

The Utility Examination Guidelines ("Utility Guidelines") create a framework for determining whether claimed subject matter complies with 35 U.S.C. § 101. Utility Examination Guidelines, Federal Register 66(4):1092-9 (January 5, 2001). The Utility Guidelines instruct the PTO to refrain from rejecting the claims under 35 U.S.C. § 101 if the claimed subject matter possesses a "well established utility" because "a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention ... and the utility is specific, substantial, and credible." Utility Guidelines at 1098. If no "well established utility" exists then the PTO should determine if the Appellants have "asserted . . . any specific and substantial utility that is credible." Utility Guidelines at 1098. Again the Utility Guidelines instruct the PTO to refrain from rejecting the claims under 35 U.S.C. § 101 if the Appellants have asserted a specific utility which is not a "throw away [utility] . . . such as the use of a complex invention as landfill." Utility Guidelines at 1098. The Utility Guidelines instruct the PTO to assess credibility "from the perspective of the one of ordinary skill in view of the disclosure and any other evidence of record . . . [and the PTO] must treat as true a statement of fact made by an applicant in relation to the asserted utility, unless countervailing evidence can be provided that shows that one of ordinary skill in the art would have a legitimate basis to doubt the credibility." Utility Guidelines at 1098-9.

The Supreme Court held that a claim to a method for producing a chemical compound where future research would have to be performed to determine a use for the compound, lacked utility. Brenner, Comr. Pats. V. Manson, 148 U.S.P.Q. 689, 696 (1966)(hereafter "Brenner"). In so finding, the Court focused on whether more research would be needed *to ascertain whether* the compound had *any utility*. Id. at 695. The Court emphasized that the patent system relates to "the world of commerce rather than to the realm of philosophy" to support why merely using a

claimed compound or process to determine if the claimed compound or process had any use fails to meet the utility requirement. Id. at 696 (citing In re Ruschig, 343 F.2d 965, 970 (C.C.P.A. 1965).

The PTO recognized what the Brenner Court meant when it provided the guidelines outlined in The Manual of Patent Examining Procedure ("MPEP") regarding using a claimed process or compound in a research setting. The MPEP states:

> Many research tools such as gas chromatographs, screening assays, and nucleotide sequencing techniques have a clear, specific and unquestionable utility (e.g., they are useful in analyzing compounds). An assessment that focuses on whether an invention is useful only in a research setting thus does not address whether the specific invention is in fact "useful" in a patent sense. Instead, Office personnel must distinguish between inventions that have a specifically identified utility and inventions whose specific utility requires further research to identify or reasonably confirm. (emphasis added)

Manual of Patent Examining Procedure, Edition 8 (E8), at § 2107.01 (relying on Brenner).

(iii) The Specification Provides a Credible Asserted Utility for the Subject Matter of Claims 53-61, 71, and 72

A stated by the Examiner, it is not required that the Appellants demonstrate a utility, only that the Appellants assert a credible utility. Thus, Appellants need only provide a credible utility for the method itself. This utility can be based on the importance of the mechanism on which the method is based or the credible real world uses for compounds that might be identified by the method. The Appellants direct the Board's attention to page 3, lines 12-21 of the specification, wherein the Appellants disclose:

> In a first aspect, the invention features a method of treating granulocytopenia in a subject, including administering to the subject an agent that inhibits the degradation of GM-CSF mRNA, thereby treating granulocytopenia in the subject. In various embodiments of the first aspect of the invention, the granulocytopenia is relative or absolute; the degradation of GM-CSF mRNA is inhibited by inhibiting the mRNA degradative activity of TTP; or the agent that inhibits the degradative activity of TTP is a competitor of TTP. For example, the competitor can compete with TTP for binding on the AU-rich element (ARE) of GM-CSF mRNA; or the competitor can compete with TTP for binding on an mRNA degradative enzyme.

Thus, the utility of the compound identified by the provided method is explicitly asserted. The attention of the Board is further directed to page 20, lines 12-29, wherein the Appellants disclosed:

> Increased levels of GM-CSF are provided by inhibiting the degradation of GM-CSF mRNA. This is accomplished by inhibiting the mRNA degradative activity of certain proteins identified herein as having GM-CSF mRNA degradative activity.
>
> Herein it is shown that tristetraprolin (TTP) stimulates degradation of GM-CSF mRNA (see, e.g., Examples 1 and 4). Without being bound by theory, the mRNA degradative activity of TTP is likely to be a function of its ability to recruit a deadenylating enzyme into proximity with the GM-CSF mRNA. Thus, an agent that inhibits the degradation of GM-CSF mRNA can be an agent that inhibits the mRNA degradative activity of TTP, for example, a competitor of TTP. A competitor of TTP can compete with TTP for binding to the AU-rich element (ARE) of GM-CSF mRNA, thereby partially or completely inhibiting the binding of TTP (or a TTP-like protein) to the AU-rich element. Alternatively, a competitor of TTP can compete with TTP for binding to an mRNA degradative enzyme (e.g., a deadenylase, exonuclease (e.g., a 3' exonuclease) or endonuclease) that plays a role in TTP-induced GM-CSF mRNA degradation. Examples of the agents that inhibit TTP induced mRNA degradation include certain mutant TTP molecules described herein. Other agents, such as chelators of zinc, can also inhibit TTP's mRNA degradative activity.

Thus, the showing that (1) granulocytopenia can be treated by increasing levels of GM-CSF, and (2) TTP binding to the ARE of GM-CSF mRNA stimulates degradation, is sufficient credible evidence that a compound that inhibits the binding of TTP to an ARE could be useful in treating granulocytopenia. Therefore, a method that can be used to identify compounds that inhibit the binding of TTP to an ARE must also be useful. For example, data are provided on pages 61-106 of the specification, such as for example page 100, lines 9-19, demonstrating the degradation of the TNF-α mRNA ARE by TTP. Further, the data provided on page 38, lines 14-22, demonstrating the accumulation, prolonged expression, and lack of the deadenylated form of GM-CSF mRNA in TTP-deficient cells in response to stimulus, establish that GM-CSF mRNA is degraded by TTP. These data, in view of the known role of GM-CSF in granulocytopenia (Nemunaitis, J. Drugs. 1997 Nov;54(5):709-29, attached), provide a clear and credible indication that an inhibitor of GM-CSF mRNA degradation could be identified for use in treating granulocytopenia. Further, the attached Declaration Under 37 C.F.R. § 1.132 filed on August 24,

2005 by one of skill in the art at the time the application was filed attests that the claimed method has a scientifically credible utility based on the data presented in the specification.

(iv) The Examiner's Arguments Are Based on an Incorrect Legal Standard

The Examiner states that "[i]n order for the claimed method to have utility, the method must give rise to a product that satisfies the utility requirement ..." The Examiner then argues that "the specification does not teach where any compound has been identified by the claimed method, much less that the product so identified has in fact been found to satisfy the utility requirement, either directly or indirectly."

This is not a proper statement of the requirement for providing a utility for a screening method. It is the method itself, i.e., a method of finding a compound that can or may interfere with binding between TTP and ARE, for which utility must be shown. There is no requirement that a compound be identified for a method of looking for a compound that can or may impact a known disease pathway to have a real world utility. Those of skill in the art will recognize that a method of finding a compound that interferes in the disclosed pathway is valuable and has utility. This position is supported by the MPEP, which states "[m]any research tools such as ... screening assays ... have a clear, specific and unquestionable utility (e.g., they are useful in analyzing compounds)." Manual of Patent Examining Procedure, Edition 8 (E8), at § 2107.01. The Examiner is requiring a standard of utility that goes beyond that provided in the MPEP and by the courts for a screening method.

The Appellants further point out that, as the choice of compound to apply to the screening method is variable, exemplification of the method, wherein a specific compound is identified and described, would not, and could not, be evidence that any other compound existed. Thus, the implication that the utility of a screening method depends on the actual identification of a useful compound, does not make sense. Rather it is the capability of the method to identify such a compound should one exist, that is the basis for utility of a screening method. Appellants establish this capability through the teaching of the mechanism of TTP and ARE interaction.

(v) The Examiner's Evidence and Arguments Do Not Establish that the Subject Matter of Claims 53-61, 71, and 72 Do Not Have a Credible Asserted Utility

The satisfaction of the utility requirement can be met by showing that a person of ordinary skill in the art would appreciate that the asserted utility is specific, substantial, and credible. To this end, the attached Declaration Under 37 C.F.R. § 1.132 filed on August 24, 2005 by one of skill in the art at the time the application was filed attests that the claimed method has a scientifically credible utility based on the data presented in the specification. In contrast, the Examiner has cited no specific basis to contradict Appellants' assertion of utility. Thus, it should be accepted as sufficient. Because this rejection is believed to be overcome, its withdrawal is respectfully requested.

(C) Rejection of Claims 53-61, 71, and 72 35 U.S.C. § 112, first paragraph, as not having utility

Claims 53-61, 71, and 72 stand rejected under 35 U.S.C. § 112, first paragraph, as not supported by a credible asserted utility or well-established utility. Appellants respectfully traverses this rejection. The Examiner bases this rejection on the reasons set forth in the rejection under 35 U.S.C. § 101. The Appellants therefore traverse this rejection for the reasons set forth above.

(8) SUMMARY AND CONCLUSION

The Appellants have demonstrated that each claim on appeal is enabled. The nature of the invention and the relative skill of those in the art are such that the amount of direction or guidance presented and steps that were exemplified in the specification are sufficient to enable the skilled artisan to practice the screening method without undue experimentation.

The Appellants have also demonstrated that each claim on appeal is supported by a specific, substantial, and credible utility.

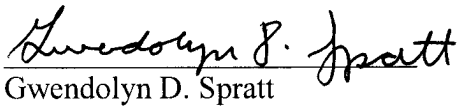
For the foregoing reasons, Appellants submit that the claims 53-61, 71, and 72 are patentable.

A Credit Card Payment authorizing payment in the amount of $500.00 for the fee for a large entity under 37 C.F.R. § 41.20(b)(2) is made electronically herewith. This amount is

believed to be correct; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

NEEDLE & ROSENBERG, P.C.



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(9) CLAIMS APPENDIX

53. A method of identifying a compound that modulates the binding of a tristetraprolin (TTP) or a TTP-like polypeptide to an AU-rich element (ARE), comprising:

a) contacting a sample containing the TTP or the TTP-like polypeptide and an ARE with the compound, and

b) detecting or measuring the binding between the ARE and the TTP or the TTP-like polypeptide, whereby an increase or decrease in the binding between the ARE and the polypeptide, relative to the binding between the ARE and the polypeptide in the absence of the compound, identifies a compound that modulates the binding of TTP or a TTP-like polypeptide to an ARE.

54. The method of claim 53, whereby an increase in the binding between the ARE and the polypeptide identifies a compound that stimulates an activity of a TTP or a TTP-like polypeptide.

55. The method of claim 54, wherein the method identifies a compound that stimulates degradation of an mRNA molecule comprising an ARE.

56. The method of claim 55, wherein the mRNA molecule encodes tumor necrosis factor-α (TNF-α).

57. The method of claim 53, whereby a decrease in the binding between the ARE and the polypeptide identifies a compound that inhibits an activity of TTP or a TTP-like polypeptide.

58. The method of claim 57, wherein the method identifies a compound that inhibits degradation of an mRNA molecule comprising an ARE.

59. The method of claim. 55, wherein the mRNA molecule encodes granulocyte-macrophage stimulating factor (GM-CSF) or IL-3.

60. The method of claim 53, further comprising contacting the sample with an inhibitor of mRNA transcription prior to detecting or measuring the binding between the ARE and the polypeptide.

61. The method of claim 53, wherein the ARE is a class II ARE.

71. The method of claim 58, wherein the mRNA molecule encodes TNF-α.

72. The method of claim 58, wherein the mRNA molecule encodes GM-CSF or IL-3.

(10) EVIDENCE APPENDIX

List of Evidence Involved in Appeal

1. Nemunaitis, J. Drugs. 1997 Nov;54(5):709 ("Nemunaitis")
2. Declaration Under 37 C.F.R. § 1.132 by Jack D. Keene ("Keene Declaration")

Statement of Entry in the Record

Appellants submit herewith copies of evidence for use in the appeal. Documents 1-2 (Nemunaitis and Keene Declaration) were submitted by Appellants in the August 24, 2005 response to the April 25, 2005 Office Action.

(11) RELATED PROCEEDINGS APPENDIX

None